## Remarks

Declaration

The declaration was marked in ink by the inventor to change the street address to 33 from 139. The zip code is correct.

Amendments to the Specification

Page 10 has been amended as requested by the examiner. No difference in the cases of the letters describing the figures was observed, either in the brief description nor in the text, relative to the labeling of the formal drawings.

Rejections under 35 U.S.C. §112

Claim 17 was rejected as indefinite and non-enabled. Claims 17 and 18 have been cancelled solely to facilitate prosecution.

Rejections under 35 U.S.C. §102

Claims 1-7 were rejected under 35 U.S.C. §102(a) over Rigotti, et al., Curr. Opin. Lipiol. 8, 181-188 (1997). Claim 8 was rejected under §102(b) over Spona, et al., Contraception 54, 299-304 (1996). Claims 8, 12, and 13 were rejected under §102(b) as disclosed by Bajetta, et al., Br. J. Cancer. 70, 145-150 (1994). Claims 9, 12, and 14 were rejected under §102(b) as disclosed by Cirkel, Human Reproduction 11, 89-101 (1996). Claims 10 and 11 were rejected under 35 U.S.C. §102(b) as disclosed by Whitcroft and Stevenson (1992). These rejections are respectfully traversed if applied to the amended claims.

The claims have been amended to be specific to a method of treatment of individuals in need of alteration of the production of reproductive hormones (see last paragraph of page 12) by

alteration of expression of SR-BI or binding by SR-BI of cholesterol or cholesteryl ester to alter transport of cholesterol or cholesteryl esters to steroidogenic tissues for treatment of disorders in which the levels of reproductive hormones are involved (second and fourth paragraphs of page 13).

The claims have also been amended to require specific alteration of SR-BI expression or binding. This excludes the general treatment using estrogen (see page 11, lines 2-9). While it has been observed that estrogen affects cholesterol blood levels, this alone does not make obvious that there is any affect on SR-BI. It was only after applicant specifically observed the effect of knocking out SR-BI expression in animals on their reproductive abilities, that one could draw the corollary that this made for a way to treat disorders associated with reproductive hormone levels.

None of the art cited by the examiner discloses nor makes obvious such a method.

Rigotti, et al., teach that SR-BI mediates transfer of cholesteryl esters. However, since this typically involves an excess of steroid production, it does not follow that this would be a means that could produce a therapeutic effect, nor that one should treat the now claimed class of patients. No where does Rigotti disclose nor lead one to select these patients as a class in need of treatment.

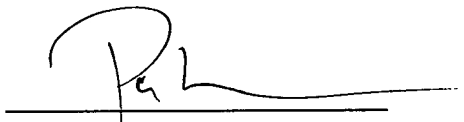
Similarly, the art disclosing the affect of estrogen on cholesterol or SR-BI expression does not lead one to the conclusion that this could be used to alter hormone levels in a useful manner. The missing element in all of this art, at a minimum, is that one cannot demonstrate or make obvious that altering SR-BI levels or binding will produce a meaningful effect on hormonal levels. *This is particularly true since estrogen is not used as a method for preventing*

*high cholesterol (nor has such an effect been established) which is the precusor that must be transferred by SR-BI to result in steroid production, as required for production of reproductive hormones.* These remarks are application to Spona, Bajetta, et al., Cirkel and Whitcroft. In none of these cases is the method of treatment (administration of estrogen or derivative thereof) a means of *selective* alteration in expression of SR-BI or binding by SR-BI, as required by the claims.

In contrast, applicant's study with knockout animals is very specific and demonstrates that effective alterations in hormonal levels can be achieved.

Allowance of claims 1-16 is therefore earnestly solicited. All claims as pending upon entry of this amendment are attached in an appendix for the convenience of the examiner.

Respectfully submitted,



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Dated: June 16, 2000

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